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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,675	01/27/2005	Graham Cotton	PA0254	1801
22840	7590	05/05/2006	EXAMINER HAQ, SHAFIQUA	
GE HEALTHCARE BIO-SCIENCES CORP. PATENT DEPARTMENT 800 CENTENNIAL AVENUE PISCATAWAY, NJ 08855			ART UNIT 1641	PAPER NUMBER

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/522,675	COTTON, GRAHAM
	Examiner Shafiqul Haq	Art Unit 1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 20 March 2006.  
 2a) This action is FINAL. 2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-21 is/are pending in the application.  
 4a) Of the above claim(s) 7,9,11 and 14-21 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-6,8,10,12 and 13 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 27 January 2005 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>1/27/05</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

**DETAILED ACTION**

***Response to Election/Restrictions***

1. Applicants' election of Group I, Claims 1-10, 12 and 13 filed March 20, 2006 in response to Office Action dated February 24, 2006 is acknowledged and entered. Since the election is made without traverse, the restriction requirement is deemed proper and is made FINAL.
2. Applicants' elected a single species compound as disclosed in page 12 of Applicants' remarks/arguments filed March 20, 2006 and claims 1-6, 8, 10, 12 and 13 read on the elected species. Accordingly, Claims 7, 9, 11 and 14-21 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.
3. Claims 1-6, 8, 10, 12 and 13 are examined on merits.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claims 1-6, 8, 10, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. With respect to claims 1 and 2, it is unclear what is meant by the term "derivative thereof" i.e. it is unclear what additional structural and functional features are required for a cyanine dye to be an acceptable "derivative".

7. With respect to claim 1, it is not clear what groups are encompassed by the phrase "a group suitable for covalent reaction with a thioester" because "suitable groups" are not disclosed or defined in specification.
8. Claim 2 is vague and indefinite because the recitation of "adapted for" with respect to M is not clear as to how M is modified for attachment to F.
9. The term "optionally include one or more groups" in claim 2 render the claims indefinite because the term "optionally include one or more groups" is not a positive recitation and may be interpreted as groups not being a required component of the claimed invention.
10. The language "which may be optionally substituted with sulphonate" in claim 8 of line 6 renders the claim indefinite because the term "optionally" is not a positive recitation and the suiphonate group may be interpreted as a group not being a required component of the claimed invention.
11. The language "optionally no more than two atoms" in claim 10 of line 8 renders the claim indefinite because the term "optionally" is not a positive recitation and "optionally no more than two atoms" may not be a required component of the claimed invention.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kopia et al (US 5,667,764).

Kopia et al disclose compounds of formula (I) and formula (II) (column 11) comprising a chromophore {e.g. cyanine. See formula (II)} linked to a bioaffinity tag B through a spacer R<sub>2</sub> wherein the linker comprises functional linkages (target bonding group) for coupling to proteins or peptides (column 11, lines 1-67; column 14, lines 46-60 and formulas IV and IX). Kopia et al disclose several functional groups on spacer L<sub>2</sub> comprising amide, hydrazone, amine, anhydride, carbonyl, amidine and triazine and at least one of them anticipates a group "suitable for covalent reaction with thioester" as claimed in present application.

Therefore, the reference is deemed to anticipate the cited claim.

#### ***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 2-6, 8, 10, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopia et al (US 5,667,764) in view of Schuler et al (Bioconjugate Chem 2002).

Kopia et al disclose compounds of formula (I) and formula (II) comprising a chromophore {e.g. cyanine. See formula (II)} linked to a bioaffinity tag B through a spacer R<sub>2</sub> wherein the linker comprises functional linkages (target bonding group) for

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coupling to proteins or peptides (column 11, lines 1-67; column 14, lines 46-60 and formulas IV and IX). Kopia et al. also disclose that the invention relates to use of the compounds for site-specific delivery of therapeutic and diagnostic agents (e.g. labeled dye) in vivo (column 1, lines 20-22) and this site-specific delivery would require different types or functional groups that reacts with specific desired proteins or biomolecules on the target.

Kopia et al, however, do not disclose functional group comprising carboxylic acid thioester and a 1, 2-aminothiol group.

Schuler et al in a method to label polypeptide containing cysteine, disclose using carboxylic acid thioester group to label peptides or proteins (see abstract and page 1039, lines 7-10 of right column). Schuler discloses that the thioester group is especially useful for its highly specific interaction with proteins and peptides containing N-terminal cysteine residue (page 1040, lines 14-17 of right column and scheme 1 and 2 of page 1041).

Therefore, given the above fact that thioester containing functional group is common and known in the art (Schuler et al) to specifically bind or locate proteins or peptides containing N-terminal cysteine, it would have been obvious at the time of the invention to a person of ordinary skill in the art to substitute thioester group for other functional group on R<sub>2</sub>, in the compound of Kopia et al for specific labeling of proteins or peptides containing N-terminal cysteine, because Kopia's site specific labeling would require different types or functional groups for reaction with specific desired proteins or biomolecules on the target.

The features of the dependent claims are also described by the references. As for claims 3-5, Kopia et al disclose spacer  $R_2$  that comprises groups or atoms (see definition of  $R_2$  in column 11, lines 47-67) and at least one of them is the same as the linkers  $L^1$  and  $L^2$  of present application. As for claim 6, Kopia et al disclose biotin for affinity tag (column 12, lines 65-67) and as for claim 8, Schuler et al disclose thioester group (e.g. benzyl thioester) that is same as the thioester group of claim 8 when  $R''$ =aryl or arylkyl.

#### ***Double Patenting***

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-6, 8, 10, 12 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 8-9 of copending Application No. 10/241,333. Although the conflicting claims are not

identical, they are not patentably distinct from each other because claims 1-5, 7, 9 and 11-12 of copending application are drawn to a compound comprising essentially the same composition as claimed in the cited claims of instant application.

As for example, in copending application, B is bioaffinity tag which is encompassed by affinity tag of present application and carboxylic acid thioester group of present application is encompassed by thioester group of the copending application.

Therefore, it would be obvious to one of ordinary skill in the art to include equivalent bioaffinity tag for B and other equivalent thioester group in the compound of copending application with the expectation of obtaining similarly useful dye labeled thioester containing compound for detection and isolation of biomolecules with a reasonable expectation of success.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 1-6, 8, 10, 12 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7, 9-12 and 15-16 of each of 1) copending Application No. 10/241,355 and 10/522,665 in view of 2) Kopia et al (US 5,667,764).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-6 and 8-9 of copending application are drawn to a compounds comprising a fluorescent dye linked to a affinity tag through a linker or

spacer wherein the linker or spacer comprises a target bonding group selected from thiester and 1,2-aminothiol group.

The compounds of copending application differ from present compounds only by having a different dye in the compound i.e. compounds of copending application comprise an acridone or a quinacridone dye whereas compounds of present application comprise a cyanine dye.

Kopia et al disclose compounds of formula (I) and formula (II) comprising a chromophore {e.g. cyanine. See formula (II)} linked to a bioaffinity tag B through a spacer  $R_2$  wherein the linker comprises functional linkages (target bonding group) for coupling to proteins or peptides (column 11, lines 1-67; column 14, lines 46-60 and formulas IV and IX).

Since cyanine dye is very common and known in the art (Kopia et al) for its high extinction coefficients and reasonable resistance to photodegradation, it would have been obvious at the time of the invention to a person of ordinary skill in the art to substitute acridone or quinacridone dye with quivalent cyanine dye, in the compound of copending application, with the expectation of obtaining a similarly useful compound for detecting or isolating labeled biomolecules.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

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19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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